Reviewer’s report

Title: Characterization of Salmonella enterica from invasive bloodstream infections and water sources in rural Ghana

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Reviewer: Craig W. Hedberg

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The authors present a study to examine the potential for local water sources to provide a reservoir for invasive Salmonella infections in a region of rural Ghana. The study focused on the characteristics of 165 Salmonella isolates obtained from 2,720 blood cultures taken from children from 2007-2012, and on 22 Salmonella isolates collected from 511 water samples from across the region, during a 3-month period in the middle of the overall study period. In general, there was a much greater serovar diversity among the water isolates, and little overlap in serovars between water and human isolates. PFGE analysis of 76 blood culture isolates demonstrated some clonality and clonal clustering. 58% of blood culture isolates were considered to be multi-drug resistant and 5 o 12S. Enteritidis were found to have reduced susceptibility to ciprofloxacin.

The authors concluded that human-to-human transmission was unlikely, "but [that their results] rather indicates a vast variety of different sources of infection." However, their data clearly suggest that water, the only source they looked at, was not a likely source for the observed invasive infections. One of the limitations of the study that was not discussed was any epidemiologic information on the cases. Thus, no exposure data was presented. No data on use of antibiotics, either as risk factor for infection or as a predictor of resistance is presented.

The degree of PFGE clustering could well be indicative of human-to-human transmission. One interesting comparison that could have been made would have been a PFGE analysis of the 57 S. Typhi isolates obtained. What degree of PFGE clustering would have been seen among these isolates? Since they would have come from a human reservoir, a comparison to the observed patterns in the NTS may have been instructive.

Specific comments:

p. 7 line 102 The time frame for the blood cultures listed on p. 9 lines 155-156 should be moved here. They are methods, not results.

p. 7 line 112 The time frame for the water samples listed on p. 10 line 175 should be moved here.

p. 8 line 125 Was there any epidemiologic data available for analysis?

p.8 line126 What does "pre-select possible identical genotypes" mean?

p.9 line 159 Why not analyze the Typhi isolates by PFGE as a comparison to the NTS?
p. 13 line 212-213 It should be noted that FQ resistance is primarily related to S. Enteritidis. This could be a function of S. Enteritidis source or response to treatment with ciprofloxacin.

p. 13 lines 218-220 The conclusion that human-to-human transmission is unlikely does not seem justified by the data as presented. There is no time function in the PFGE data, and PFGE is not as reliable as WGS for this type of study to explore genetic relatedness of the isolates.

p. 15 line 263 The conclusion is overstated. The lack of any epidemiologic data limits what can be inferred from the microbiological data.

**Are the methods appropriate and well described?**
If not, please specify what is required in your comments to the authors.

No

**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

No

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